International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

Central Management of Sugar, Amino Acid, Fat and Cholesterol are Strategic Approach and Achieved by Targeting Pre Prandial Prior Nutrition with Moderate Intensive Exercise and Post Prandial Moderate Intensive Exercise with Prandial Nutrition Containing Sugar and Type of Fatty Acids, Brain Hypothalamus Arcuate Nucleus

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Abstract: ***Pre and post prandial moderate intensive timely exercise, prior pre and post prandial nutritional containing esters of fatty acids in triglyceride and LDLc play a major part in management of metabolic diseases according to their saturated and unsaturated (both mono and poly) fatty acid contents producing different type of metabolic disorders. A vital role in maintaining metabolic homeostasis and preventing disorders. The gastrointestinal tract serves as the primary control point for nutrient absorption, with glucose being a key factor in the development of ectopic fat deposits, particularly in the liver & pancreas. Unregulated glucose absorption leads to inflammatory conditions, contributing to metabolic disorders like fatty liver disease and atherosclerosis. Effective glucose management strategies, including inhibiting specific transporters and performing pre and post meal exercises, can help control postprandial glucose levels, reduce ectopic fat deposits, and maintain overall metabolic health. This article explores various management approaches aimed at sustaining calorie balance and preventing metabolic dysfunctions.***

Keywords: Pre and post prandial moderate intensive exercise, 3 doses of prior pre-prandial nutrition (Break-fast, Lunch and Dinner), brain hypothalamus arcuate nucleus**, Metabolic** homeostasis, calorie, postprandial glucose, metabolic disorders, ectopic fats, glucose transporters, SGLT1, Glut 2. GLP1R, Insulin RA, GIPRA insulin RA, GIPRA, triglyceride LDLc.

1. Introduction

Nutrition with calorie management for carbohydrate, protein and fats are most important for metabolic homeostasis to prevent metabolic disorders. Nutrition with calorie management is better than to burn calorie by exercise. For E.g. in River water management, we construct dam in the river origin for quality distribution of water throughout the year. But it will never be achieved only managing river tributaries at periphery without constructing dam in river. Similarly, central management nutrition (sugar, amino acid, fat with cholesterol) are most important, fruitful and meaningful as dam in river rather than managing alone sugar and fat etc at the periphery in blood as in managing river tributaries peripherally.

When we take food, all foods together gather in GI tract, from there it will pass through intestinal lumen (which act as barrier) between GI and enterocyte. Then it passes from enterocyte to blood circulation. Here we can say that intestinal tract is the origin of the river gathering all foods together and intestinal wall serves as dam, The carbohydrates, fats and protein are transferred to amino acid, fatty acids and glucose, fructose etc. by different types of digestive enzymes and then these fatty acids, amino acids and glucose transported to enterocyte and from enterocyte it is again transported to blood circulation as river flow from the dam.

After transport to blood circulation, amino acids, fatty acids and glucose are stored in their defined destination in the body. Fat is stored in adipose tissue and amino acid in protein synthesis and glucose in liver and muscles. In body the storage capacity $_1$ of fat, as per the kcal is 1,40,000 and as per the weight 15.5 kg in body. Amino acid storage as per the kcal is 24,000 and as per weight is 12 kg. Glucose storage as per kcal 800-1000 and as per the weight is 250 gm –400 gm. So, any amount of fat taken by body can be easily adjusted to their respective storage areas with negligible alteration of storage capacity. But, as glucose storage capacity is 250 gm in normal condition, an average human being of 70 kg weight and 100 mg/dl fasting sugar and in between the meals and 4 hours after meal the glucose amount in blood circulation will be 5 gm only and this change varies as per their weight. So, after taking a meal which contains approx. 90 gm of glucose the total glucose amount in blood circulation will be 95(90+ 5) gm and this 95 gm should have to come to basal level to 5 gm within 2 hours of taking a meal (prandial sugar).

At best and maximum 3-4 hours of post prandial period, it should come to basal state i.e. 5 gm.

As the glucose is transported to liver according to their concentration gradient in portal circulation and this process is independent of insulin and transport depends upon glut 2 transporter .The glucose taken by liver is deposited as

glycogen dependent on availability of insulin and the highest capacity of liver for glycogen storage is 100 gm and it is already 80 % fill up before a meal period, so after glucose absorbed in liver the rest 20 % will be filled up as glycogen in the liver and i.e. within 2 hours (prandial period) . The rest glucose which is not stored as glycogen are converted to saturated fatty acid from sugar by hepatocytes and it depends on glycolysis by hyperinsulinemia (more insulin level blood than normal level) for de novo lipogenesis in post prandial periods producing mostly 16 carbon saturated palmitic fatty acids which is highly pro inflammatory with different cytokines, leukokines, chemokines etc. It attracts macrophages & T cells, lymphocytes by producing IL1, IL6, IL17 etc. and the fats in the liver transferred to a chronic inflammatory cell producing organ by activating immunological process by macrophages and T cells and different hormonal imbalance by adipokines and these are the main culprits to produce metabolism disorder in the body. All these fats lead to steatosis, steatohepatitis , cirrhosis and carcinoma of liver and also main culprit to produce production of small particle LDL with compact 16,14 carbon saturated fatty acid esters of cholesterol and these atherogenic cholesterol esters also activated to form LPa in liver which when enter in the blood circulation by VLDL deposited in the endothelial tissue of arteries and arterioles etc. and thereby, disarranging their structure and production of chemokines signalling factors. They attract macrophages, T cells etc. thereby producing atherosclerosis of arteries and arterioles. So, it is necessary to manage glucose homeostasis at the time of origin in GI tract and during the time of blood circulation after the meal (prandial period) to avoid fats as well as ectopic fats deposit in liver and pancreas to avoid metabolic disorder.

Amino Acid:

As negligible source of energy from amino acid metabolism required for calorie homeostasis only 0.08 to 1.2 gm / kg of body weight is required for body maintenance purpose & amino acids are building block of protein which are essential for countless biological Process and amino acids are reusable in the body by cycling process & minor amounts of amino acids are metabolised to nitrogen products like creatinine, uric acid & urea etc. as there is no special reserves store for amino acid. All the extra amino acid consumed in diet are converted to 14,16 carbon atherogenic saturated fatty acid in liver by insulin dependent glycolysis due to high level of insulin present in postprandial period and these 14,16 carbon atherogenic and inflammatory saturated fatty acid are incorporated to glycerol to produce triacylglycerol (triglyceride) and due to their inflammatory and atherogenic activities, small partial LDLc ,LPa etc produced by the process of LCAT in HDLC and ACAT in microphases and other cells .These cholesterol esters of 14,16 carbon saturated fatty acid is deposited in endothelial layer and taken by macrophage giving rise to accumulation of cholesterol esters forming foam cells and ultimately producing atherosclerosis plaque (HDLc cannot take back to liver as do in normal cells) and the 14,16 saturated fatty acid esters in phospholipid of cell membrane produce dysfunction of lipid raft elasticity fluidity etc and their by producing cell dysfunction.

N. B.-Branched chain plant-based protein are good for liver function, but all essential amino acids are not available in a single plant-based protein diet but available in animal protein. So, all type of cereal containing 'moong dal',' aarhar dal', 'masoor dal', red and green gram dal should be taken together in diet to reduce progression of hepatic encephalopathy fibrosis and cirrhosis and in sarcopenia to get muscle mass building. In CKD it should be restricted as it will produce more nitrogen waste product giving rise to fibrosis of kidney.

Fats (Fatty Acid and Cholesterol):

After fatty acid is collected from liver and dietary fats in GI tract, Fatty acids are to be esterified with glycerol and free cholesterol to produce triglyceride and cholesterol ester respectfully. Also, cholesterol collected by HDLC from periphery to be esterified to make it more hydrophobic and they will go to the centre of the HDLC making membrane of HDL free to accept more cholesterol. from periphery by HDLc and there by improve HDL functions and capacity. Also, HDLc carry cholesterol from macro phage to avoid foam cell formation and HDLc take all these esterified cholesterols to LIVER for excretion purpose in bile, thereby, reducing cholesterol level in blood. Triglyceride are used to supply fats for energy production in different cells and organs. And also, this triglyceride is stored in adipose tissues for future energy. Cholesterols carried by VLDL from Liver and Chylo Micron from GI tract are delivered to their destination cells such as steroidogenesis cells to produce steroid hormones and gonadal cells to produce sex hormones also to the skin to produce vitamin D. And in cell it gives structure and also it produces bile acid for digestion.

NB: In room temperature saturated fatty acids take longer time, while mono-unsaturated fatty acids take moderate time and poly-unsaturated fatty acids take shorter time. Such types of disintegration/break down are also manifested in the body.

Triglyceride in blood are esters of saturated unsaturated (mono and poly) fatty acid, and the saturated fatty acids are from 4 to 22 carbon straight chain producing sort chain (4to8) healthy for gut micro biota immunity and health. Medium chain fatty acid 12 to18 carbon where 14 and 16 are atherogenic and 12 and 18 are neutral.

Triglyceride in blood containing esters of monosaturated fatty acids are better substrate for mitochondrial respiration with cellular health benefit by reducing oxidative stress and cell apoptosis etc.

Triglyceride in blood containing polyunsaturated such as omega 3 are of a linolenic acid, EPA and DHA are most important in cellular functions: linolenic acid derived from plant source converted to EPA and DHA also EPA can be converted to DHA. EPA acts mostly peripherally by improving fatty acid oxidation transportation and activate PPARA receptors and thereby improving fatty acid metabolism and triglyceride turnover. DHA act on CNS producing good memories and improve cognitive Alzheimer's and other functions like improving child brain growth and development in pregnancy and childhood.

Triglyceride containing omega 6 produce arachidonic acid in cell membrane. They produce inflammatory Interleukins and cytokines for acute and chronic inflammation.

Cholesterol from Dietary source and from endogenous sources produced by liver, adrenal glands, intestine and reproductive organs. But majority are from liver source. Cholesterol from GI tract transported in blood by chylomicrons. Cholesterol produced in liver transported by VLDC.As free cholesterol are toxic to intracellular structures producing their dysfunction, structural damage, oxidative stress. So, the cholesterol stored in the cells and cholesterol transported in blood are to be esterified to cholesterol ester for better sustenance and by that reduce toxicity of free cholesterol. Due to their hydrophobic nature they migrate to core portion of HDLc so the membrane will be free from free cholesterol and more cholesterol can be collected from periphery to liver.

Cholesterol transported to liver via VLDL and HDLc are secreted in bile as cholesterol and bile acid or recirculation in VLDL. Cholesterol esters may be from saturated unsaturated (mono and poly fatty acids) and work according to their fatty acid contents the cholesteryl ester is delivered to reproductive organs, adrenal glands including all steroidogenesis cells as poly unsaturated fatty acids and thereby, the cholesterol is easily free to produce hormones in regular basis. Cholesterol ester from monounsaturated acid received by cell is easily taken by mitochondria to produce energy. Cholesterol of saturated fatty acid are difficult to be metabolise and their life span is more than any other cholesteryl ester. By this nature they are mostly comparted with small LDLc particles and APOB-100 saturated low density lipo-protein and thereby their longer life span than others. They are often impaired and oxygenated and glaciated etc. macrophages in endothelial cells cannot take native LDLC but when this saturated small LDLc are impaired or oxygenated they are easily taken by the macrophage. The impaired cholesterol cannot be taken back by HDLc to Liver. So, this saturated cholesterol ester is deposited in macrophage forming a large number of intra cholesteryl esters and there by producing all inflammatory activities and macrophage apoptosis and necrosis producing plaque, fibroatheroma foam cell etc.

Native LDLc are not atherogenic and cannot be taken by macrophage in endothelial cells of arteries and arterioles. But impaired or disfunction LDLc carrying cholesteryl esters along with apoB100 bind to proteoglycan producing auto immune pro-inflammatory antigen complex. And this antigen complex is suitable to be taken by scavenger receptors of macrophages. And all these activate innate immunity cell such as macrophage, neutrophil, dendrite cells etc. and also activate adaptive immunity cell such as CD4T subsects CDTH1 & TH2, TH17 etc. producing interferon IL1, IL6, IL17, TNFa etc. and changing endothelial cells of arteries and forming it a auto immune inflammatory organs by activating M1 type of macrophages and this process continue for a long period from childhood to old age producing atherosclerosis. But it can be checked by CDTH2 and T-Reg cells by producing IL4, IL10 and IL13 thereby anti-inflammatory and antiatherogenic M2 macrophage.

Atherosclerosis fibroatheroma and plaque by accumulating number of cholesteryl esters and other toxic materials producing necrosis degeneration and apoptosis of surrounding cells. It promotes lipid deposit in the surrounding area thereby transformation of macrophages to phenotype M1.

N.B- High LDLc and high triglycerides in blood are not atherogenic and their atherogenic effects are to be measured in respect to their esters of saturated and unsaturated fatty acids contains producing bad or good effect.

Triglycerides and cholesteryl esters containing unsaturated (mono and poly) fatty acid are easily de-esterified after reaching their target cell or organ producing free cholesterol, free fatty acid and free glycerol but cholesteryl esters containing saturated fatty acid are not easily de-esterified and their long survival period and long-time exposure to epigenetic factors made them impaired and dysfunctional LDLc. This impaired LDLc binds with proteoglycan in arterial wall transforms to a antigen complex which activates innate immunity.

Fat from diet source is better than lever source as they contain all type of saturated and unsaturated fatty acid. but in liver hepatocyte produce mostly 14,16 carbon atherogenic fatty acids from sugar and amino acid.

Triglyceride containing esters of mono, and poly unsaturated fatty acids and they are good for health benefits.

LDLc containing cholesteryl esters of mono, and poly unsaturated fatty acids are good for health benefits and also prevent atherosclerosis. But LDLc containing saturated fatty acid are bad for health benefit and unsaturated fatty acids are non-atherogenic.

LDLc receptor recycle hundred times in normal conditions to transport cholesterol into liver cells but binding PCSK9 enzymes at the receptor will make a complex which cannot be recycled but will be degraded in lysosomes by lysosomal acid lipase. And this PCSK9 enzyme can be inhibited to bind to LDLc receptor by monoclonal antibodies. And PCSK9 enzyme production can be reduced by inhibiting transcription of MRNA of PCSK9 by activation of MiRNA in nucleus. But both these two methods will help in reducing the numbers and binding capacity of PCSK9. But, have no effect on production of LDLc receptor or production of cholesterol in lever and only for the purpose of to complete normal recycling that is hundred times of a LDLc receptor.

Cholesterol Metabolism

Free cholesterol is toxic to cell and in order to make it to non-toxic and more stable it is converted to cholesteryl ester by LCAT or ACAT. Esterifying a fatty acid from the phospholipid present in cell. Apo A-1 is the structural and potent active catalyst for cholesterol metabolism and Apo A-1 take up cholesterol and Phospholipid from its production sides such as liver, intestine, macrophages, fibroblast etc. and delivery to targeted cholesterol receiving organs or cells and thereafter at the end to liver for excretion

in bile. Whereas ApoB-1 100 and 48 are potent and backbone of structural protein for VLDL which carry fats soluble vitamins phospholipids cholesterol etc. for delivery to destinated organs or cell. Apo E is the delivery boy of helping delivery of these product fat cholesterol etc from VLDL and HDLC and work as a ligand to respective receptors of destinated organ/cells in the body.

Function of HDLC with APO A-1 on cholesterol metabolism:

Apo A-1 is the structural protein of HDLC and after its formation from endoplasmic reticulum in the cell it collects cholesterol and phospholipids from that cell by the process cholesterol efflux mediated by ABC A-1 and ABC G-1 present in that cell.

- It produces inert nontoxic cholesterol ester by L-CAT in HDLC collecting a fatty acid from the phospholipid in that cell.
- It transfers cholesteryl ester to VLDL, IDL, LDL etc of containing APO B-100 and APO B -48

To transfer the cholesterol to be used in targeted required cells as well as for excretion in liver for recycled or to excreted in bile.

HDLC with the APO A-1 distribute cholesterol to different peripheral cells such as steroidogenesis cells, adrenal glands, testis, ovary etc. by SRB 1 receptors. Also, finally all the cholesterols delivered to lever for excretion in bile. APO A-1 is not used or endocytosed by these cells, and it remain intact and for this APO E mediated for the transport and endocytosis of cholesterol.

In arterial wall the deposited LDLc binding to proteoglycans form a antigenic complex to produce innate immunity response by activating macrophages and other adaptive immunity to produce atherosclerosis in that particular wall.

VLDL fat transported to all cells, organs and, tissues to supply energy from fat sources and supply of VLDL fat depends on available triglycerides percentage in volume with respect to total volume in VLDL. VLDL triglycerides containing more than 15 per cent can be transported to different parts. Here only APOE and not APOB100 take part in transporting and improving fatty acid metabolites transcription factors for VLDL receptors, lipo-protein lipase receptors, PPRA receptors and thereby improving uptake of fatty acids in adipose tissues, muscle tissue and other cells.

VLDL carrying less than 15 per cent triglycerides in volume are called LDLc and here APPOB-100 is main ligand with APPO E to present total VLDL particle to LDLc receptor in lever for endocytosis and make them different product such as amino acids, fatty acids, cholesterol to end the VLDL metabolism.

70-80 percent of cholesterol are produced in liver and also 70-80 percent of cholesterol are taken by liver LDLC receptors to excreted in bile or for recycling. This production and taken off - cholesterol by hepatocytes of liver are dependent on free cholesterol level and number of receptors in hepatocytes and they are inversely proportional, i.e., free cholesterol reduced in hepatocytes will increase receptors and vice versa. By reducing free cholesterol and increasing receptors will reduce cholesterol in the blood.

Cholesterol Homeostasis or Management

1) Cholesterol can be managed at the site of their production internally at the liver and externally at GI tract from dietary source and bile source. Bile source 1000mg and dietary source 300mg approx. total in the range of 1000-1500 mg can be blocked by ezetimibe by blocking cholesterol absorbing receptor in GI Tract and bile acid recycling from the GI Tract to portal circulation can be inhibited by cholestyramine. There by giving rise to more production of bile by liver. Above procedure will reduce the cholesterol level in liver cells and enhancing cholesterol receptor numbers in liver cells and decrease the blood level of cholesterol for improving bile production.
2) Utilisation of cholesterol in gonadal and steroidogenesis cells and production of Vitamin Dand cellular structure etc. are natural way.
3) Cholesterol formation in liver can be inhibited by statins by inhibiting HMG COA reductase in cytosol of liver cells and thereby reducing the availability of free cholesterol in hepatocytes there by increasing more LDL receptor and more collection of cholesterol from blood reducing blood cholesterol.

N.B.: Ezetimibe and cholestyramine together produce catalytic effect on reduction of blood cholesterol and increase cholesterol excretion in bile and thereby improving quality, numbers, and function of HDLc to collect cholesterol from periphery cells and transfer to liver for excretion in bile or for recirculation.

Improved function of HDLC will increase transform of cholesterol esters from LDLC to HDLC via CETP enzyme and LDLc with low content of cholesterol are easy substrate/ligand for liver cells to clear and effective excretion in bile in the form of cholesterol and bile acid.

- Ezetimibe and cholestyramine are catalyst for enhancing natural process of cholesterol excretion in GI track and neutral to fatty acid absorption. So, they keep the nature intact.
- Statin and PCSK9 are used to reduce cholesterol production and LDLc receptors by inhibiting or promoting some enzymes involved in cholesterol production. But their intermediate metabolites products may be ligands for increase or decrease of some cellular products.

Management- 1

Better Nutritional management with pulse nutrition (Prior pre-prandial and prandial meal) therapy with a combination of protein and mono saturated fatty acid in the diet & minimum 30 mins prior or before to each pre-prandial $_2$ meal counting approx. 3 times of pre-prandial pulse nutritional therapy, minimum 30 min. before each 3 major meals (breakfast, lunch and dinner).

For example, prior pre-prandial pulse nutrition therapy should contain the type of protein use in the diet. Suppose we select pulses plant protein (‘moong dal’, ‘arhar dal’, red

gram, green gram etc.) the percentage of protein in these are approximately 25%. If each time, we take 20 grams any of these pulses it will give you only 5 grams of available protein as per their 20-gram weight. So, taking 2 grams of all pulses plant proteins in three pulses pre-prandial nutrition (breakfast, lunch and dinner). A total 15 grams of protein will be available in a day from these three-pulse pre-prandial nutrition. Then balance 45 to 60 grams of protein should be collected from dietary source or adding additional protein such as whole milk cheese, paneer, egg etc. to these three-pulse pre-prandial nutrition therapy. Thereby produce better health benefit. These three-pulse nutritional therapy should be differently prepared for better health benefit.

1) Prior pre-prandial breakfast nutrition therapy
   Total 20 grams moong and red gram seeds should be germinated in night and that sprouts should be taken with 35 grams of whole milk cheese.
2) Prior lunch pre-prandial nutritional therapy
   'Arhar dal' or 'moong da'l of 20 grams and 35 grams of milk 'paneer'.
3) Prior dinner pre-prandial nutrition therapy
   20 grams of red gram 'chhatua' and 2 eggs without yolk

NB: Water or liquid intake in the pre-prandial nutrition and before meal will delay the cephalic phase of priming the digestive system i.e. in normal condition after taking a meal it's liquid portion with carbohydrate and protein enter the small intestine in the Bolus form for a period of 20 minutes. after food intake. Then food in stomach becomes pasty and semi solid and they pass in a linear row to the small intestine. After these cephalic phases of 20 minutes. CCK from neuro-endocrine cells and pepsin in the stomach are produce and they give rise to satiety and also reduce hunger before taking original meal and thereby decrees nutrition calorie intake in breakfast, lunch and dinner.

3. Prior pulse pre-prandial monounsaturated nutrition therapy in breakfast, lunch and dinner per day.

EXAMPLE- 10 TO 15 ml mustard oil adding to the food will give rise to 20 to 40 grams of triglyceride in breakfast, lunch and dinner pulse nutrition therapy. Mustard oil, olive oil, and peanut oil contain 60% monounsaturated fatty acid, 21% polyunsaturated fatty acid and 12% saturated fatty acid.

Our body required 200 grams of fatty acid daily producing 1800 kilocalories out of 2000 required calorie per day for a normal human.

Total 40 grams fats are available from breakfast, lunch and dinner pulse nutritional therapy, and rest 160 grams should be from the dietary fats and converted saturated fat from glucose source.

NB:

1) Addition of mustard oil direct to suitable fruit and salad etc. will improve its taste and flavour.
2) Fried food should be prepared from either mustard oil of peanut oil as their smoking point is the higher than other oil.
3) Mustard peanut and the olive oil are with same amount mono saturated fatty acids range from 50% to 60% and thereby producing equal health benefit to heart, mitochondria, and beta-oxidation so higher metabolic benefit.
4) All oil should be selected from cold processed preparation rather than refined oil to produce more metabolic benefits.

Pleotropic effects of monounsaturated pulse nutritional therapy:

a) Reduce gastric motility
b) Increase GIP, GLP1 AND CCK production.
c) Produce satiety and reduce hunger.
d) Reduce insulin resistance in periphery.
e) Decreases triglyceride and LDL level in blood.
f) Improve diabetes profile.
g) It is a better substrate for mitochondrial respiration, function and health conditions better than poly unsaturated and saturated fatty acid.
h) Reduces inflammation and is an immune modulator.

Pleotropic effects of pulse nutritional pre-prandial therapy with protein and monounsaturated fatty acids 30 min prior to meal intake Will prime digestive system in the following ways:

1) It will increase secretion of GIP and GLP1 as protein & fats are more potent than carbohydrates for incretin secretion such as GLP1 and GIP.
2) GLP1 improves glucose dependent insulin secretion and reduce glucagon secretion in the pancreases.
3) GIP improves fat metabolism in adipose tissue by improving & proliferating GIP receptors in adipose tissue for fat metabolism purpose and there is no GLP1 receptors in adipose tissue.
4) GIP encourage glucagon secretion in pancreatic cells and thereby creating an atmosphere of low energy environment with thermogenic heat production and less production of ATP in electron transfer chain of mitochondria and hence reduce mitochondrial oxidative stress and increase its function.
5) 30 mins before taking protein and mono saturated fatty acid combination will increase HCL secretion thereby encouraging more cleaving of long chain protein to short chain amino acids protein fractions in the stomach.
6) Fatty acids prime B cells of pancreases to produce more secretion of insulin if it is required in post prandial glucose homeostasis.
7) Fatty acids also prime CCK secretion in producing more bales, pancreatic exocrine secretion, and HCL secretion there by enhancing digestive system activities.
8) GIP receptor agonist GIPR is a better substrate for improving aerobic fatty acid B oxidation and improvement of BAT proliferation & improve thermogenic heat production & reducing ectopic fat deposit in different organs thereby reducing chronic inflammatory immune reactions.
9) Monosaturated Fatty acid is a better substrate for aerobic B oxidation than other saturated & ploy

unsaturated fatty acid so increasing mono saturated fatty acid consumptions will help for improvised aerobic B oxidation & mitochondrial oxidative stress & improve in total mitochondrial function.

Management 2

In the GI tract we can limit glucose absorption from GI tract to enterocytes in small intestines by blocking – inhibiting SGLT-1[3] transporter which is 90% responsible for glucose transport from intestinal lumen to enterocyte. SGLT-1 is expressed in luminal border of GI tract and a non-absorbable SGLT-1 inhibitor can be given with meals to prevent glucose absorption from small intestine to enterocyte without producing any adverse effect as it is not absorbed in blood stream.

Management 3

From enterocyte glucose will be transported (approx. 90%) to blood circulation by GLUT-2[4] transporter present in basolateral side of enterocyte and this GLUT-2 transporter can be inhibited or blunted for a short time say 10-15 mins by giving short half-life GLUT-2 inhibitor during the mealtime to prevent glucose absorption from enterocyte to circulation.

Pleotropic effect of GLUT-2 inhibitor

By inhibiting GLUT-2 transporter , the glucose which is taken by liver and pancreas are prohibited to enter the hepatocytes and pancreatic cells so there will be no ectopic fat deposition in liver and pancreas and thereby their function will be well maintained and there will be no mitochondrial stress effect & thereby preventing metabolism disorder and moreover due to its action on B cells of pancreas , insulin secretion will be reduced and thereby encouraging B oxidation in cellular level , as it will maintain mitochondrial health by reducing stress as aerobic oxidation is healthy for mitochondrial respiration and function and moreover GLUT-2 transport glucose from renal cells to glomerular capillaries. By blocking or GLUT-2 action on renal cells will enhance smooth passage of glucose in urine and thereby reduced insulin label and encouraging B oxidation and mitochondrial health and higher level of insulin required for muscular deposit of glucose whereas normal level of insulin is sufficient to deposit glucose in adipose tissues.

Management 4 (exercise after meal- Post prandial exercise[6])

Prandial glucose can be managed by calorie burn process thereby to reduce blood glucose level after meal, moderate muscles exercise is required which will utilize 50% max glucose capacity thereby producing energy source 50 % from glucose and 50% from B oxidation of fatty acids, but if we will improve exercise strength to use 75 % of maximum utilization then 90 % energy will be from glucose source and negligible energy from fatty acids so daily post meal exercise of 10-15 mins to reduce prandial glucose level thereby reducing ectopic fats in liver and pancreas. As the normal body use 2000 kcal per day & the source of calorie utilization in a normal condition is 90 % from the fatty acid B oxidation say 1800 kcal from fats and total amount of fats required for this used is 200 gm to get this energy & 200 kcal is used from glucose source i.e. 50 gm maximum from glucose source , we are taking a diet as glucose in a meal more than 90 gm, in total a day we are consuming more than 300 gm of glucose so by burning 50 gm glucose all the rest 250 gm use as saturated fat production of 16 carbon palmitic acid and this 16 carbon saturated fatty acid is the main substrate for B oxidation and also its accumulation causes pro inflammatory , chronic inflammatory, auto immune metabolic disorders by producing different cytokines , interleukins, adipokines etc. and activating innate and adoptive immunity .In this respect WHO Recommended total sugar from diet as well as added sugar should be 10% of total calories used daily and reducing it to 5% of total calories will give more health benefit 11 (WHO RECOMMENDATION).

Pleotropic effect of Prandial exercise.

Prandial exercise will increase abdominal pressure thereby reducing portal circulation to liver and due to increased abdominal pressure GI lumen diameter will be decreased thereby reducing nutritional absorption, in total reducing the prandial calorie intake.

Management 5 (Pre-Prandial Exercise to Improve Prandial Glucose Homeostasis)

Pre-prandial exercise[5] before 15-30 mins of a taking meal can burn glucose source of energy by doing medium to intensive exercise using 50-75% maximum oxygen capacity and by doing this it will improve the glycogen storage capacity of the liver & muscles as glucose will be utilized from glycogen store of liver & muscles thereby increasing its glycogen storage capacity in liver & muscles pre-prandially. But during night-time for a period of approx. 8 hours glycogen stored in liver is significantly reduced as glucose required for resting basal metabolic rate and for brain[10] is derived from glycogenolysis and gluconeogenesis in liver at night, so pre-prandial breakfast exercise should be replaced by postprandial breakfast exercise for better health benefits.

NB-pre-prandial exercise is beneficial in all meal except breakfast meal as there is already reduced glycogen storage in liver at night.

Fat Management[7]

Fat is the main source of cell structure producing its membrane structure by phospholipids, cholesterol & fat is the main source of steroid hormone production including vitamin D & main source of energy in the human body because 90 % energy derived from fat source , only 10% from glucose source, 80 % of saturated fat is used in B oxidation and most of this saturated fats derived from carbohydrate source so there is no need of taking more saturated fats rather mono saturated fat is better substitute than saturated fat for mitochondrial.

Respiration and thereby favourable B oxidation in mitochondria[9]. And it also promotes mitochondrial formation and function. Food should contain more unsaturated fatty acid from monosaturated and polysaturated fatty acid origin & to avoid pro inflammatory & chronic inflammatory disorder & metabolic disorder of the body omega 3 ploy unsaturated fatty acid should be taken in comparison to omega 6 fatty acids which produces

all pro inflammation, chronic inflammation & metabolic disorder so nutrition should be managed accordingly.

The best ideal fat management in the body & muscles is:
Muscles Fat content: - 1.5 % of total body weight.
1.5 to 5 % is overweight i.e. BMI from 23- 29.5.
More than 5 % of the total body weight is obese i.e., BMI more than 30%.

Body fat Content[8]:

For Males	For Females
9-15	16-24

Average Fat:

Males	Females
16- 25	20- 30

Obese:

Males	Females
>25	>35

Distribution of fats:

Males	Females
Abdominal	Thigh & buttock

2. Conclusion

In conclusion, managing postprandial glucose and overall caloric balance is essential to preventing metabolic disorders like fatty liver disease and atherosclerosis. Strategies such as inhibiting glucose transporters in the gastrointestinal tract, along with targeted exercises, can effectively control glucose levels and reduce ectopic fat accumulation in the liver and pancreas. These methods help maintain metabolic health and prevent the onset of chronic conditions by promoting better energy utilization. It is crucial to focus on early interventions, starting from nutrient absorption to sustain long-term metabolic stability.

NB-
From ancient period all placental delivered animals including human were always in a running state in their work due to fear from environmental factors such as animal, insects and etc. Due to their running state, they utilize 50-90 % of their maximum oxygen utilized capacity & thereby used their energy source from sugar i.e., 80% and 20% from fatty acids. Accordingly, their genes are made for sugar utilization & they store glycogen, and the rest remaining sugar is converted to fat, so their main source of energy was on sugar-based foods as per that present environmental condition.

At present, we hardly use our calorie requirements from sugar. Rather, 90% used from fat reserves i.e. aerobic B oxidation in mitochondria so for better B oxidation a low energy condition with low insulin & high oxygen level required. For e.g., a person requiring 2000kcal energy per day needs 1800 kcal from fat and 200 kcal from sugar per day. For getting calories 200 kcal from sugar, we require 50 gm of glucose per day. In a normal meal at present we are taking 90 grams of sugar , and in 3 meals per day we are taking 270 gm of sugar daily and our total sugar requirement is only 50 gm to give necessity calorie & considering a standard meal contains 90 gm sugar we require only 15 gm of sugar from each meal out of 90 gm in a meal so 75 gm of sugar should go to dustbin in the prandial management of sugar as they produce ectopic fats & other metabolism disorders so prandial management of sugar to be used to limit as 15 gm only in a meal. For that inhibitors are required to blunt the action SLGT 1, glut 2, pre-prandial & prandial exercise etc. to be required for creating proper environment to meet aerobic B oxidation and to keep low level of insulin, low level energy & high level of oxygen in mitochondria.

Calorie or Energy Homeostasis in Post Prandial Period and in between two Meals:
After amino acid fats and sugar enter to blood circulation. The master energy regulator in the body is hypothalamic arcuate nucleus. It contains at least two crucial populations of neurons to project to second order target including para ventricular nucleus and these neuronal activities are within few seconds, and this manage orexigenic sensitivity and anorexigenic in a co-ordinated manner. It regulates the peripheral organs involve in the central of nutrition storage and it is independent of food intake status. Insulin, GLP-1, GIP and Leptin receptors in arc urate nucleus produce negative effect and there by producing less calories and utilizing more calories by activating POMC and de activating AGOUTIC response protein neurons. Here we give the example of the clomiphene on oestrogen receptor of hypothalamus in CNS, which by attaching to the oestrogen receptor produce agonist effect of oestrogen on hypothalamus sensing as if more oestrogen is present in the blood. And this clomiphene has no remarkable effect on peripheral oestrogen receptors such as ovary, Uterus and Mammary gland etc. So, maintaining normal oestrogen activity in the peripheral without any agonist effect. Likewise, a sub strait of chemical or neurological origin (like clomiphene on hypothalamus) may be targeted or developed to act only on arcuate GLP1 or insulin GIP LEPTIN receptor etc. with their agonist effect on hypothalamus without no remarkable effect on peripheral or other CNS GLP1R or Insulin R to produce energy homeostasis in the body in future.

N.B: By pleotropic effect of insulin receptor in Arcuate nucleus it will immediately activate in few seconds brown fat (BAT). By regulating myostatin and there by immediately reduce insulin resistance in the body and it is irrespective to nutritional status.

N.B: GIP agonists are important in managing fat metabolism both centrally and peripherally Leptin agonist is most effective in fat management both centrally and peripherally.

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